

ABSTRACT

The present invention is related to enhancing the function of anti-tumor antibodies by regulating Fc γ RIIB-mediated activity. In particular, disrupting SHIP activation by Fc γ RIIB enhances cytotoxicity elicited by a therapeutic antibody *in vivo* in a human. The invention further provides an antibody, *e.g.*, an anti-tumor antibody, with a variant Fc region that results in binding of the antibody to Fc γ RIIB with reduced affinity. A variety of transgenic mouse models demonstrate that the inhibiting Fc γ RIIB molecule is a potent regulator of cytotoxicity *in vivo*.